ANNALS OF SURGERY
Vol. 233, No. 4, 549–555

Impact of Bloodstream Infection on Outcomes Among Infected Surgical Inpatients

Daniel P. Raymond, MD, Shawn J. Pelletier, MD, Traves D. Crabtree, MD, Thomas G. Gleason, MD, Timothy L. Pruett, MD, and Robert G. Sawyer, MD

From the Surgical Infectious Disease Laboratory, Department of Surgery, University of Virginia Medical School, Charlottesville, Virginia

Objective
To assess the importance of bloodstream infection (BSI) to outcomes among infected surgical patients.

Background
Bloodstream infection complicating infection is thought to connote a more serious condition compared with a primary infection alone. The authors recently reported, however, that BSI does not alter outcomes with central venous catheter colonization in the presence of sepsis. The significance of BSI with other infections has been incompletely evaluated.

Methods
Data on all episodes of infection among surgical patients were collected prospectively during a 38-month period at a single hospital, then analyzed retrospectively to determine the independent prognostic value of BSI for all infections by logistic regression analysis, and for abdominal infections and pneumonia using matched control groups.

Results
During the study period, 2,076 episodes of infection occurred, including 363 with BSI. Patients with BSI had a greater severity of illness and a greater death rate. After logistic regression, however, BSI did not independently predict death. After matching patients with abdominal infections and pneumonia with BSI to patients without BSI but with a similar site of infection, severity of illness, age, and causative organism, no difference in outcome was seen.

Conclusions
Bloodstream infection is associated with critical illness and death but appears to be a marker of severe primary disease rather than an independent predictor of outcome.

Although transient bacteremia in healthy people may be considered innocuous (e.g., with dental work), bloodstream infections (BSIs) in inpatients are associated with considerable rates of death and complications, particularly in the critically ill.[1] Many authors have attempted to quantify the impact of BSI in terms of excess deaths, hospital stays, and cost.[1–5] These studies have used various statistical techniques, although they generally rely on the matching of patients with BSI to those without. One possible shortcoming of these efforts is the use of uninfected patients as controls, leaving open to debate whether the worsened outcomes observed were from the BSI itself or from any underlying primary infection. The study of primary BSI (or BSI with an unknown source) to control for underlying infections is also less than satisfying because most primary BSIs are still thought to be secondary to an occult focus elsewhere, most commonly vascular catheters.[6]

In addition, the proximate cause of death in septic patients remains unknown. The relative roles of worsening local infection (frequently complicated by immunodysregulation) versus systemic spread of infection (heralded by bacteremia or fungemia) are unclear but germane. If the latter were more important, one would predict a higher death rate among patients with BSI compared with those with similar infections and severity of illness without BSI. We recently reported, however, that in patients with clinical evidence of infection, the addition of BSI to the finding of central venous catheter

Supported by The Surgical Infection Society Junior Faculty Award (R.G.S.).
Correspondence: Dr. Daniel P. Raymond, Box 3150, Building MR4, Lane Road, University of Virginia HSC, Charlottesville, VA 22908.
E-mail: dpr4w@virginia.edu
Accepted for publication October 3, 2000.

colonization with 15 or more colony-forming units of bacteria or fungi does not significantly affect outcome.[7]

The current study was undertaken to test the hypothesis that BSI is not an independent risk factor for death among a broader group of infected surgical patients. A large, prospectively derived database was analyzed to ascertain whether BSI independently predicted death by logistic regression analysis. In addition, patients with abdominal infections or pneumonia with BSI were matched to those with similar diseases, severity of illness, age, and causative organism but without BSI, and outcomes were assessed by univariate analysis.

PATIENTS AND METHODS

This study was approved by the University of Virginia Human Investigation Committee. Data were collected at the University of Virginia Health Sciences Center from December 1996 to January 2000. All patients on the adult general surgery, transplant surgery, and trauma surgery services were evaluated prospectively by investigators every other day by chart review, review of daily laboratory and microbiologic data, antibiotic usage, and house staff/attending interview. Patients specifically excluded from the study included those with uncomplicated, acute cholecystitis without cholangitis, nonperforated appendicitis, necrotic but nonperforated bowel (all because of probable lack of significant contamination) and orthopedic-related infections occurring on the trauma service (e.g., open fractures). Viral infections were excluded.

Centers for Disease Control definitions were used throughout,[8] with the exception of catheter-related infections (see below). Criteria for the diagnosis of pneumonia included systemic evidence of infection, purulent sputum production, isolation of a predominant organism from an appropriately obtained culture, and a new or changing infiltrate or effusion on chest radiograph. Diagnosis of a urinary tract infection required the isolation of greater than 10^5 organisms per milliliter of urine or greater than 10^4 organisms per milliliter in association with dysuria. Catheter-related infections were identified by isolation of 15 or more colony-forming units from catheter tips by the semiquantitative roll plate technique in the setting of suspected infection. Catheter tips were cultured only when removed from patients with a temperature of 38.5°C or more, or a persistently rising or elevated white cell count. We have found that under these circumstances, outcomes are similar whether BSI is documented.[7] Thus, both syndromes are included under catheter-related infections. Cellulitis, peritoneal infections, and surgical site infections were generally diagnosed clinically, frequently without cultures. Infections were considered nosocomial in origin if they were not documented or suspected at the time of admission.[8] Infectious episodes occurring more than 72 hours apart in the same patient were considered separately and individually for analysis.

Bloodstream infections were diagnosed by isolation of organisms from blood cultures from any site, with the exception of *Staphylococcus epidermidis* or other coagulase-negative staphylococci, which required isolation from two separate sites. Per protocol, patients more than 48 hours after surgery who developed a temperature of 38.5°C or more had blood cultured sterilely from two sites, at least one percutaneously. The second culture was occasionally obtained from patients with difficult access from a clean vascular catheter (generally just after placement). Cultures were repeated every 24 hours if the patient remained febrile. Blood cultures were also sent frequently, but less consistently, in the setting of normothermia or hypothermia and a rapidly rising white cell count and/or systemic hypotension. A secondary BSI was diagnosed when all bacteria or fungi (by speciation and antibiogram performed in the University of Virginia clinical microbiology laboratory) growing from blood were also cultured from the primary site. If cultures from the primary site were not done or were reported as mixed or not completely speciated, secondary BSI was diagnosed if the organism causing BSI was likely to have been present in the primary infection (e.g., *Escherichia coli* BSI in the setting of a diverticular abscess that was not cultured). A diagnosis of primary BSI was made for any bacteremia or fungemia that did not meet the criteria for secondary BSI above. No assumptions as to the actual primary site of these cryptogenic infections were made. Some patients had localized infections simultaneously with a primary BSI.

Intake variables recorded for each infectious episode at time of diagnosis of infection included age, gender, race, white cell count, temperature, the Acute Physiology and Chronic Health Evaluation (APACHE II),[9] date of admission, date and type of interventions, and time from hospital admission or diagnosis of infection until initiation of treatment. The white cell count, temperature, and APACHE II score were all the most extreme values recorded within the first 24 hours of diagnosis of infection. Other variables recorded included infection site, culture data, antibiotic regimen, duration of antibiotic treatment, and presence of significant comorbidities, including diabetes mellitus (type 1 or 2), chronic renal insufficiency (serum creatinine $\geq$2.0 mg/dL before admission), mechanical ventilator dependency (excluding the immediate perioperative period), hemodialysis dependency, coexisting malignancy, corticosteroid or other immunosuppressive therapy, blood transfusion (administration of at least one unit of cellular blood products after admission but before diagnosis of infection), history of preexisting pulmonary disease, cardiac disease, or liver disease, and presence of a solid organ transplantation.

The primary outcome variable examined was death before discharge. The secondary outcome of time from initiation of treatment to death or discharge was also noted.

Statistical analysis was performed using SAS software (SAS Institute Inc., Cary, NC) and GB-STAT Version 6.5 (Dynamic Microsystems, Silver Spring, MD). Univariate

Table 1. DEMOGRAPHIC AND OUTCOMES DATA

	No BSI	All BSI	Primary BSI	Secondary BSI
Number	1,727	363	191	172
Age (yr)	52.3 ± 0.4	50.6 ± 0.9	49.0 ± 1.2	52.6 ± 1.3
APACHE II	11.8 ± 0.2	17.8 ± 0.4*	17.6 ± 0.5	18.2 ± 0.6
Female	804 (46.6)	130 (35.8)*	73 (38.2)	57 (33.1)
Nosocomial	1,132 (65.5)	303 (83.5)*	170 (89.0)	133 (77.3)
Intensive care unit	319 (18.5)	192 (52.9)*	106 (55.5)	86 (50.0)
White cell count ($\times 10^{-3}/\mu L$)	13.4 ± 0.2	15.9 ± 0.6*	15.2 ± 0.6	16.8 ± 0.9
Max. temp. (°C)†	38.0 ± 0.0	38.8 ± 0.1*	38.8 ± 0.1	38.6 ± 0.1
Abdominal infection	469 (27.2)	55 (15.2)*	4 (2.1)	51 (29.7)
Pneumonia	346 (20.0)	120 (33.1)*	64 (33.5)	56 (32.6)
Catheter infection‡	89 (5.2)	85 (23.4)*	20 (10.5)	65 (37.8)
Urinary infection	377 (21.8)	81 (22.3)	37 (19.4)	44 (25.6)
Surgical site infection	355 (20.6)	26 (7.2)*	9 (4.7)	17 (9.9)
Days of antibiotics	10.8 ± 0.3	14.0 ± 0.7*	12.4 ± 0.6	15.7 ± 1.3
Length of stay (days)§	15.1 ± 0.5	26.9 ± 1.6*	26.5 ± 2.1	27.3 ± 2.3
Deaths	184 (10.7)	72 (19.8)*	38 (19.9)	34 (19.7)

BSI, bloodstream infection.
Percentages are in parentheses.
* $P < .001$ No BSI vs. All BSI; no other differences are ≤.05.
† Within 24 h of diagnosis of infection.
‡ Signs and symptoms of infection, no BSI, catheter tip ≥ 15 colony-forming units, no other site identified.
§ From diagnosis of infection to discharge.

analysis of categorical data was performed using chi-square testing, and continuous variables were analyzed using two-tailed Student *t* tests, with equal or unequal variances based on the F test. Values are expressed as mean ± standard error (continuous variables) or as a percentage of the group of origin (categorical variables). All probability values were two-tailed, and probability values of 0.05 or less were considered significant, except where organisms from both primary and secondary BSI were compared with non-BSI episodes, where $P \leq .025$ was considered significant as a result of the Bonferroni correction.

Logistic regression was performed to identify independent risk factors predictive of death. Univariate analysis was first performed to identify variables associated with death with $P \leq .10$; these were then used in the logistic regression model. Backward stepwise logistic regression analysis was used to estimate the odds ratio of death (dependent variable) and the presence of comorbidities or potential prognostic factors (independent variables). The odds ratio was estimated using the final logistic regression model as exponential (β-coefficient), and the 95% confidence intervals for the odds ratios were calculated. An initial Pearson correlation coefficient was determined for all continuous variables to screen for highly correlated parameters. After establishing the logistic regression model and identifying factors significantly associated with death, BSI was added to the model to identify its role as an independent predictor of death.

Matching was performed between patients with abdominal infections and pneumonia with and without BSI by site, APACHE II score ± 2 points, age ± 5 years, and class of causative organism (gram-positive, gram-negative, or fungus). Groups were then compared using univariate analysis as above.

RESULTS

As shown in Table 1, during the 38-month study period, 2,076 episodes of infection were treated, including 363 associated with BSI (172 secondary, 191 primary or cryptogenic). Patients with BSI, when compared with those without BSI, had a greater APACHE II score, white cell count, maximum temperature, duration of antibiotics, length of stay, and death rate. Patients with BSI were also more likely to be male, to be in the intensive care unit, to be diagnosed with a nosocomial infection, and to have pneumonia or a catheter-related infection. Patients without BSI had a higher percentage of abdominal and surgical site infections. Vascular catheters were the most common source of secondary bacteremia. In Table 1, the number of local sites of infection (e.g., pneumonia) associated with BSI are higher for all BSI than for secondary BSI because of the combination of localized infection and primary BSI caused by different organisms. Sites under primary BSI represent concurrent infections with organisms different from the BSI. The total percentages for sites for both all BSI and secondary BSI are greater than 100% because of cases of multiple sites of infection with the same organism.

Organisms causing infection are listed in Table 2. All

Table 2. SPECIFIC ORGANISMS CAUSING INFECTION

Organism identified	No BSI	Primary BSI	Secondary BSI
Total	1,627	245	209
All gram-positive	655 (40.3)	174 (71.0)*	119 (56.9)*
S. aureus	142 (8.7)	8 (3.3)*	19 (9.0)
S. epidermidis/CNS†	90 (5.5)	107 (43.7)*	51 (24.4)*
E. faecalis	124 (7.6)	24 (9.8)	26 (12.4)*
E. faecium	57 (3.5)	7 (2.9)	10 (4.8)
Streptococcus spp.	95 (5.8)	11 (4.5)	4 (1.9)
All gram-negative	555 (34.1)	49 (49.0)*	72 (34.4)
E. coli	113 (6.9)	9 (3.7)	16 (7.7)
P. aeruginosa	82 (5.0)	7 (2.9)	20 (9.6)*
K. pneumoniae	63 (3.9)	4 (1.6)	5 (2.4)
E. cloacae	36 (2.2)	11 (4.5)	6 (2.9)
E. aerogenes	24 (1.5)	1 (0.4)	2 (1.0)
S. maltophilia	24 (1.5)	2 (0.8)	2 (1.0)
A. calcoaceticus	23 (1.4)	7 (2.9)	7 (3.3)
C. freundii	20 (1.2)	0 (0)	1 (0.5)
S. marcescens	17 (1.0)	4 (1.6)	5 (2.4)
All fungi	233 (14.3)	13 (5.3)*	10 (4.8)*
C. albicans	131 (8.1)	5 (2.0)*	4 (1.9)*
Non-*C. albicans*	101 (6.2)	8 (3.3)	6 (2.9)

BSI, bloodstream infection.
Percentages are in parentheses.
* $P < .025$ vs. No BSI.
† Coagulase-negative *Staphylococcus*.

bacteria and fungi were speciated in the BSI groups, whereas 843 episodes of infection in the group without BSI either had final cultures interpreted as "mixed flora" or were treated without cultures. Most of these episodes were in patients with a perforated viscus, cellulitis, or surgical site infection. Compared with all speciated infections, BSI was associated with a higher percentage of gram-positive infections, particularly the *Staphylococcus epidermidis*/coagulase-negative *Staphylococcus* group. Sixty-six of the BSIs were associated with multiple organisms; the death rate for this group was 25.8%, compared with 18.5% for those with a single organism ($P = .18$ for the difference by chi-square).

Univariate analysis demonstrated that death was associated with the 17 variables listed in Table 3. After logistic regression analysis, however, only age, APACHE II score, female gender, blood transfusion, preexisting liver, pulmonary, or renal disease, malignancy, and intensive care unit treatment were found to be predictors of death (Table 4). The presence of BSI did not independently alter prognosis.

BSI has been found to have minimal impact on outcomes from catheter-associated infections,[7] the most common primary source of secondary BSI. The results of subgroup analysis for patients with abdominal infections or pneumonia, the second and third most common primary sites of infection associated with secondary BSI, are given in Table 5. Patients with BSI in addition to these primary sites had higher APACHE II scores and were more likely to be in the intensive care and to require mechanical ventilation. In addition, patients with pneumonia and BSI were less frequently female and had a higher death rate. These findings, however, still did not address the question of whether BSI in

Table 3. CHARACTERISTICS OF INFECTED PATIENTS

Characteristics	Survivors (n = 1,778)	Nonsurvivors (n = 229)	*P* Value
Age (years)	50.4 ± 0.4	61.1 ± 0.9	<.0001
APACHE II score	11.8 ± 0.2	21.1 ± 0.5	<.0001
Female gender	782 (44.0)	112 (48.9)	.10
Max. white cell count (cells/μL)*	13.1 ± 0.2	17.2 ± 0.8	<.0001
Admission to treatment (days)	7.7 ± 0.4	22.3 ± 1.9	<.0001
In ICU at diagnosis	338 (19.0)	136 (59.4)	<.0001
Nosocomial infection	1,146 (64.5)	205 (89.5)	<.0001
Transfusion	530 (29.8)	176 (76.9)	<.0001
Cardiac disease	283 (15.9)	62 (27.1)	<.0001
Chronic renal insufficiency	122 (6.9)	23 (10.0)	.08
Hemodialysis	174 (9.8)	69 (30.1)	<.0001
Pulmonary disease	143 (8.0)	30 (13.1)	.01
Mechanical ventilation	261 (14.7)	101 (44.1)	<.0001
Malignancy	213 (12.0)	67 (29.3)	<.0001
Liver disease	110 (6.2)	43 (18.8)	<.0001
Corticosteroid therapy	446 (25.1)	71 (31.0)	.05
Bloodstream infection	297 (13.2)	64 (18.4)	.008

Percentages are in parentheses.
* Within 24 hours of diagnosis of infection.

Table 4. LOGISTIC REGRESSION ANALYSIS FOR PREDICTORS OF DEATH

Characteristic	Odds Ratio (95% confidence interval)	*P* Value
Age (per year)	1.04 (1.03–1.05)	.0001
APACHE II score (per point)	1.12 (1.09–1.56)	.0001
Transfusion	2.57 (1.61–4.08)	.0001
Malignancy	2.75 (1.78–4.24)	.0001
Female gender	1.65 (1.17–2.33)	.005
Liver disease	2.12 (1.19–3.80)	.01
Pulmonary disease	1.73 (1.05–2.84)	.03
Chronic renal insufficiency	1.85 (1.03–3.31)	.04
In ICU at diagnosis	1.70 (1.01–2.86)	.05
Bloodstream infection	0.83 (0.55–1.25)	.39

addition to a severe primary infection resulted in significant excess death. Because the sample sizes were inadequate to perform multivariate analysis, patients with and without BSI were matched by primary site of infection, APACHE II score, age, and class of infecting organism (gram-positive bacteria, gram-negative bacteria, or fungus), as shown in Table 6. The predominant infecting organism could be matched in 42 abdominal infections and 35 pulmonary infections. After matching, there were no significant differences for either site in terms of length of stay or death rate. Power analysis revealed that 1,034 patients with abdominal infections would need to be studied to confirm the small difference in the death rate found between the BSI and no-BSI groups. Because the number of deaths in patients with and without BSI were identical for patients with pneumonia, it was impossible to perform power analysis accurately.

DISCUSSION

The presence of BSI has been shown to be associated with worse outcomes in multiple studies of infected patients.[1–5] The excess rates of death and complications associated with BSI in addition to a serious primary infection, however, are much less clear. The data presented suggest but do not prove that outcomes from infection are associated mostly with the severity of the underlying disease, rather than the presence or absence of BSI, similar to our findings regarding infected vascular catheters.[7]

One difficulty inherent in the study of BSI is that blood cultures themselves have neither a 100% sensitivity nor specificity for bacteremia or fungemia. First, not every patient with an infection had blood cultures taken. Second, some patients with negative blood cultures undoubtedly had BSIs that were undetected. Third, some patients with a single isolate of *S. epidermidis* discounted as a contaminant probably had true BSI. We have, therefore, more accurately shown that a positive blood culture (obtained and interpreted in a standard manner) does not have independent prognostic significance, and perhaps our original hypothesis regarding BSI itself remains untested. It can be argued, on the other hand, that subclinical BSI or BSI undetectable by routine procedures would be even less likely to affect outcome, and we were, in fact, assessing the importance of only the most severe BSI to death. Until more sensitive measures of BSI become available, however, blood cultures remain the standard reference test and may be considered a reasonable approximation of the true BSI rate.

Most studies of BSI have used uninfected control groups for comparison and have concluded, as did we, that BSI is

Table 5. ANALYSIS OF ALL ABDOMINAL INFECTIONS AND PNEUMONIAS

	Abdominal Infection		Pneumonia	
	No BSI	BSI	No BSI	BSI
Number	479	46	406	39
Age (yr)	53.3 ± 0.8	56.7 ± 2.7	50.3 ± 0.9	52.2 ± 2.7
APACHE II score	12.3 ± 0.3	17.5 ± 1.0*	17.4 ± 0.3	21.9 ± 1.3*
Female	218 (45.5)	18 (39.1)	153 (37.7)	8 (20.5)*
Nosocomial	229 (47.8)	24 (52.2)	359 (88.4)	36 (92.3)
Intensive care unit	48 (10.0)	12 (26.1)*	236 (58.1)	30 (76.9)*
Mechanical vent.	34 (7.1)	8 (17.4)*	190 (46.8)	26 (66.7)*
White cell count ($\times 10^{-3}/\mu$L)	15.7 ± 0.4	18.6 ± 1.5	15.6 ± 0.4	20.6 ± 3.2*
Max. temp. (°C)†	38.0 ± 0.0	38.3 ± 0.2*	38.5 ± 0.0	38.5 ± 0.2
Days of antibiotics	12.4 ± 0.4	20.3 ± 4.2*	12.8 ± 0.9	16.9 ± 1.8
Length of stay (days)‡	18.1 ± 1.0	23.2 ± 3.3	24.1 ± 1.2	37.7 ± 5.9*
Deaths	52 (10.9)	9 (19.6)	86 (21.2)	14 (35.9)*

BSI, bloodstream infection.
Percentages are in parentheses.
* $P < .05$ vs. No BSI, same site.
† Maximum temperature within 24 h of diagnosis of infection.
‡ From diagnosis of infection to discharge.

Table 6. ANALYSIS OF ABDOMINAL INFECTIONS AND PNEUMONIAS MATCHED BY AGE, APACHE II SCORE, AND CAUSATIVE ORGANISM

	Abdominal Infection		Pneumonia	
	No BSI	BSI	No BSI	BSI
Number	46	46	39	39
Age (yr)	56.2 ± 2.7	56.7 ± 2.7	52.7 ± 2.7	52.2 ± 2.7
APACHE II score	17.4 ± 1.0	17.5 ± 1.0	21.6 ± 1.1	21.9 ± 1.3
Female	19 (41.3)	18 (39.1)	12 (30.8)	8 (20.5)
Nosocomial	30 (65.2)	24 (52.2)	37 (94.9)	36 (92.3)
Intensive care unit	8 (17.4)	12 (26.1)	29 (74.4)	30 (76.9)
Mechanical vent.	8 (17.4)	8 (17.4)	22 (56.4)	26 (66.7)
White cell count ($\times 10^{-3}/\mu L$)	19.0 ± 1.7	18.6 ± 1.5	16.2 ± 1.4	20.6 ± 3.2
Max. temp. (°C)†	38.1 ± 0.2	38.3 ± 0.2	38.5 ± 0.1	38.5 ± 0.2
Days of antibiotics	14.0 ± 1.4	20.3 ± 4.2	12.1 ± 1.1	16.9 ± 1.8*
Length of stay (days)‡	25.7 ± 3.6	23.2 ± 3.3	28.7 ± 3.6	37.7 ± 5.9
Deaths	11 (23.9)	9 (19.6)	14 (35.9)	14 (35.9)

BSI, bloodstream infection.
Percentages are in parentheses.
* $P < .05$ vs. No BSI; all other differences $> .20$.
† Within 24 h of diagnosis of infection.
‡ From diagnosis of infection to discharge.

associated with a greater severity of illness and death. Whether BSI is an independent predictor of death after controlling for severity of illness is less clear. Kollef et al[10] studied 2,000 intensive care unit (ICU) admissions, including both infected and uninfected patients, and found that BSI was not an independent predictor of outcome by logistic regression analysis. Digiovine et al[5] matched infected and uninfected ICU patients by severity of illness and found no difference in ICU survival, although patients with BSI did have longer ICU stays and higher costs.

Our logistic regression analysis similarly demonstrated that in a large group of infected patients, BSI was not predictive of outcome when one accounted for other significant factors, such as severity of illness and age. These data, however, do not by themselves exclude the importance of BSI in determining outcome, because it is possible that a secondary BSI, rather than the primary infection, causes the greater severity of illness found in nonsurvivors and therefore negates the prognostic value of the BSI itself. Our data in patients with abdominal infections and pneumonia where patients were closely matched by severity of illness, age, and organism, on the other hand, argue against this hypothesis, because there were no significant differences in outcome based on the presence or absence of BSI. Although no firm conclusions regarding the pathophysiology of death among infected patients can be made, these findings imply that death is more dependent on the severity of the local, primary infection than a systemic spread of identifiable microorganisms. This hypothesis (if correct) further suggests that future initiatives in the treatment of infection, whether antimicrobial or immunologic, perhaps ought to be focused more on the localized infection rather than on the global immune response.

These data, taken as a whole, do not diminish the importance of blood cultures in the clinical care of patients. More than half of all patients with bacteremia or fungemia had a primary or cryptogenic BSI that prompted treatment that otherwise would not have been rendered if blood cultures had not been obtained. Even though some of these episodes may not have been clinically significant, the associated death rate of almost 20%, similar to that seen with secondary BSI, makes it impossible to ignore BSI in the absence of an identifiable primary source. In addition, the finding of bacteremia or fungemia must trigger a more aggressive search for a primary focus of infection and must suggest other interventions, such as the replacement of central venous catheters. Finally, any positive culture data are useful in terms of changing or narrowing the spectrum of antibiotics used in a frequently critically ill patient population.

In summary, BSI, as assessed by standard blood culture techniques, does not appear to worsen outcomes beyond those predicted by the severity of the underlying infection. However, blood cultures continue to be a valuable diagnostic test because BSI is a useful marker of a greater severity of illness, and the primary source of infection causing BSI may not always be easily determined.

References

1. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1994; 271:1598–1601.
2. Smith RL, Meixler SM, Simberkoff MS. Excess mortality in critically ill patients with nosocomial bloodstream infections. Chest 1991; 100:164–167.

3. Bates DW, Pruess KE, Lee TH. How bad are bacteremia and sepsis? Outcomes in a cohort with suspected bacteremia. Arch Intern Med1995; 155:593–598.
4. Leibovici L, Samra Z, Konigsberger H, et al. Long-term survival following bacteremia or fungemia. JAMA 1995; 274:807–812.
5. Digiovine B, Chenoweth C, Watts C, et al. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. Am J Respir Crit Care Med 1999; 160:976–981.
6. Leibovici L, Konisberger H, Pitlik SD, et al. Bacteremia and fungemia of unknown origin in adults. Clin Infect Dis 1992; 14:436–443.
7. Pelletier SJ, Crabtree TD, Gleason TG, et al. Bacteremia associated with central venous catheter infection is not an independent predictor of outcome. J Am Coll Surg 2000; 190:671–680.
8. Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988; 16:128–140.
9. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985; 13:818–829.
10. Kollef MH, Sherman G, Ward S, et al. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest 1999; 115:462–474.